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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,075	03/19/2004	Jeffrey D. Johnson	090446-0200	7921
82137	7590	01/07/2009		
Metabolex, Inc. C/O Foley & Lardner LLP 975 Page Mill Road Palo Alto, CA 94304-1013			EXAMINER CHONG, KIMBERLY	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 01/07/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/805,075	Applicant(s) JOHNSON ET AL.	
	Examiner KIMBERLY CHONG	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21 and 35-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21 and 35-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/02/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 10/02/2008 has been considered. Rejections and/or objections not reiterated from the previous office action 07/02/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/02/2008, claims 21 and 35-37 are pending and currently under examination in the application.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 103

The rejection of claims 21 and 35-37 under 35 U.S.C. 103(a) as being unpatentable over Meyers et al. (US 20020009779), Newgard et al. (US Patent No. 5/854,067, hereinafter referred to as 'Patent '067') and Liang et al. (J. of Biological Chemistry, 1990. Vol. 265: 16863-16866) is maintained for the reasons of record in the Office action mailed 07/02/2008.

Applicant's arguments filed 10/02/2008 have been fully considered but they are not persuasive. Applicant cites the Yang et al. reference as evidence that only glucokinase regulates insulin secretion and that inhibition of glucokinase reduces insulin

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secretion and this teaching is supported by Liang et al. who teach that it is only glucokinase that was found to regulate glucose induced insulin secretion. Applicant further argues that Newgard (Patent '067) teach that inhibiting lowKm hexokinases in turn lowers insulin secretion and therefore concludes the results are contrary to the instant invention which suggest inhibition of hexokinase V in pancreatic cells can result in increased insulin secretion.

Applicant's arguments are not convincing. First, nowhere in the Yang et al. reference does it state or is implied that "only glucokinase regulates insulin secretion and that inhibition of glucokinase reduces insulin secretion." Yang et al. discusses glucose regulation and the role glucokinases have in the development of obesity. Nonetheless, Yang et al. was not used as a prior art reference and given the reference was published after the filing date of the instant application, this is not conclusive evidence that one of ordinary skill in the art would not want to inhibit hexokinase activity in identifying an agent for treating diabetic or pre-diabetic individuals at the time of filing of the instant invention.

It is unclear what Applicant's point is in stating that Liang et al. also teach that only glucokinase was found to regulate glucose induced insulin secretion. Liang et al. does not teach the instantly claimed hexokinase and was not relied upon for this teaching. Moreover, nowhere in Liang et al. does it state or is implied that "only glucokinase regulates insulin secretion. The fact that Liang et al. recognized that hexokinases are involved in regulation of glucose-induced insulin secretion would lead one of ordinary skill in the art to use the methods to monitor the response of glucose in

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methods of identifying agents for treating diabetic or pre-diabetic individuals along with methods taught by Meyers et al. and Patent '067.

Applicant points to column 11 and column 19 for evidence that Newgard (Patent '067) teach hexokinases lower insulin secretion, however a cursory review of these pinpoint sites do not state that inhibition of hexokinases lower insulin secretion. What Patent '067 does teach is that increased levels of hexokinase can cause insulin secretion to occur at glucose concentrations below the physiological threshold and teach that some degree of inhibition of hexokinase is optimal to improve the response to glucose, which is the claimed invention. Applicants further argue that the teachings of Newgard et al. apply to design of artificial cells and not to the direct treatment of patients with hexokinase inhibitors as claimed. The instant claims are drawn to methods of identifying agents for treating diabetic or pre-diabetic individuals and given the method "comprises" the steps listed in claim 21, this does not preclude the use of treatment steps taught by Newgard et al. Moreover, one of skill in the art would have wanted to use an pancreatic islet cell in the assay taught by Meyers et al. because Patent '067 teach the importance of islet cells in the recognition of glucose and these cells are critical to the control of blood glucose uptake and therefore the islet cell would be an important cell to determine the response to glucose in diabetic subjects.

Applicants argue that Meyers et al. do not provide any factual evidence regarding the existence or expression levels of hexokinase V in pancreatic cells and no conclusion can be drawn linking hexokinase V to glucose-induced insulin secretion in pre-diabetic or diabetic pancreatic cells and without such a link, there can be no reasonable

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expectation that inhibiting hexokinase V will result in enhanced glucose-induced insulin secretion as claimed.

This argument is not convincing because first, the claims are not drawn to inhibition of hexokinase V such as to result in “enhanced glucose-induced insulin secretion.” The claims are drawn to a method of identifying an agent comprising determining the level of glucose-induced insulin secretion and selecting the agent that improves the response to glucose which encompasses any change, however slight, in the response. Secondly, Meyers et al. was not relied upon to conclusively teach a link between hexokinase V and glucose induced insulin secretion, otherwise Meyers et al. would have been used in a 102 rejection. Meyers et al., in combination with Patent '067 and Liang et al. teach the instant method would have been obvious to one of ordinary skill in the art. Meyers et al. identified the instantly claimed hexokinase, 50365 polypeptide, has glucose phosphorylating activity and teach a method of identifying candidate test compounds or agents which bind to said polypeptide. It would therefore have been obvious to try the novel hexokinase polypeptide taught by Meyers et al. in an assay for identifying agents for treating a diabetic individual having impaired glucose-induced insulin secretion given Patent '067 teach the role of hexokinases have in diabetes and the importance of inhibiting the activity of hexokinase in methods of treating impaired glucose induced insulin secretion. One would have wanted to identify agents that could inhibit the novel hexokinase identified by Meyers given Meyers et al. and Patent '067 teach hexokinases are important for normal glycolytic activity and irregularities in their function can lead to disorders such as diabetes and further

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controlling expression of such enzymes could improve an individual's response to treatment of diabetes.

One of skill in the art would have reasonably expected to be able to use the novel hexokinase taught by Meyers et al. in an assay to identify agents for treating a diabetic individual given hexokinases are known to play a role in diabetes and given Meyers et al. teach said novel hexokinase has homologous regions to known hexokinases with the known activity of glucose phosphorylation.

Thus, the invention as a whole is *prima facie* obvious to one of skill in the art and the rejection is maintained for the reasons stated above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
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